REMARKS

Premature Finality of the Office Action

A Petition Under 37 C.F.R. § 1.181 was filed September 29, 2002, requesting withdrawal of the finality of the Office Action. The Petition was granted January 3, 2003. Therefore, the finality of the Office Action mailed July 29, 2002 is withdrawn.

Information Disclosure Statement

In the text of the previous Office Action mailed January 2, 2002, the Examiner acknowledged Information Disclosure Statements filed in August and October 2001. However, the Examiner has only initialed and returned Information Disclosure Statements filed in October 2000 and August 2001. Applicants respectfully request that an initialed copy of the Second Supplemental Information Disclosure Statement, filed October 2, 2001, be returned in the next Office Action.

Priority Claim Under 35 U.S.C. 119(e)

Applicants once again note that priority is claimed to U.S. Provisional Application No. 60/160,258 filed October 19, 1999 and U.S. Provisional Application No. 60/174,227, filed January 3, 2000. The priority claims have not been acknowledged in an Office Action. The Examiner is respectfully requested to acknowledge the priority claims in the next Office Action.

Rejection of Claims 2-18 Under 35 U.S.C. § 103(a)

A. Summary of the Rejection

The Examiner has rejected Claims 2-18 as being obvious over U.S. Patents No. 5,496,545 (Holmes-Farley, *et al.*; hereinafter "the '545 Patent") and 4,302,440 (John, *et al.*; hereinafter "the '440 Patent"). The Examiner states that as shown by the '545 Patent, a tableted composition consisting of a phosphate-binding agent and a crosslinking agent would have been known to one of ordinary skill in the art. The Examiner acknowledges that the '545 Patent does not disclose using 95% of an aliphatic amine polymer. However, the Examiner states that because the crosslinking agent is present in an amount of from 0.5% to 75% by weight, the phosphate-binding polymer is present in an amount of up to 99.5% by weight. The Examiner states that it would have been obvious to combine the '545 Patent and the '440 Patent, in order to provide a coating for a tablet containing an aliphatic amine polymer.

B. Summary of the '545 Patent

The '545 Patent discloses polymers capable of removing phosphate from the gastrointestinal tract. The '545 Patent additionally discloses a method of removing phosphate from the gastrointestinal tract, which involves administering a pharmaceutical composition of a phosphate-binding polymer. The '545 Patent teaches that pharmaceutical compositions can be in the form of capsules, tablets, pills, powders, and others. However, the '545 Patent does not teach the proportion of polymer in a tablet or capsule. Also, the '545 Patent does not teach the desirability of minimizing the amount of excipients in a pharmaceutical composition. Significantly, the '545 Patent does not teach how to prepare a tablet with greater than 95% of an aliphatic polymer.

C. Summary of the '440 Patent

The '440 Patent discloses a method for preparing a thinly-coated aspirin tablet, which does not disintegrate in the stomach materially slower than an uncoated aspirin tablet. The preferred coating comprises hydroxypropylmethylcellulose and a plasticizer. The '440 Patent does not disclose tablet formulations of a polymer and, in particular, does not disclose whether a polymer tablet can be coated with a composition disclosed therein.

D. Claims 2-18 Are Not Obvious

The Examiner asserts that the '545 Patent teaches that a crosslinking agent is present in a tablet. This assertion is incorrect. Essentially no crosslinking agent is present in the tablets of the '545 Patent or in the instantly claimed tablets. Crosslinking agents are only present in the reaction mixture to prepare polymers disclosed in the '545 Patent. No crosslinking agent is present in the final polymer; the chemistry of the crosslinking agents is described below.

No crosslinking agent is present in a tablet or other pharmaceutical formuations because it reacts with a polymer to form the crosslinking groups that connect the polymer backbones (crosslinked polymers are recited, for example, in present Claims 5, 7 and 12). That is, the crosslinking agent forms the crosslinking groups which are **an integral part of the polymer**. Support for this assertion is found at column 4, line 47 to column 5, line 16 of the '545 Patent, which teaches that polymers can be crosslinked by adding a crosslinking agent to the reaction mixture during polymerization or by reacting the polymer with a difunctional crosslinking agent after polymerization. Following reaction, a molecule of crosslinking agent becomes a

crosslinking group in the polymer. Since crosslinking groups are part of the polymer, they are not a second element in the composition, as asserted by the Examiner, but rather a part of the first element, i.e., the polymer drug.

Moreover, crosslinking agents such as epichlorohydrin (disclosed at column 5, lines 5 to 7 of the '545 Patent) cannot be present in a pharmaceutical formulation because they are highly toxic and are suspected cancer agents, as is shown in the enclosed copies of the Aldrich chemical catalog (Exhibit A) and a material safety data sheet (Exhibit B). Thus, the presence of greater than trace quantities of a crosslinking agent would render a pharmaceutical composition unacceptable for administration to a patient. Thus, residual crosslinking agent is removed prior to formulation of the polymeric drug. This supports the contention that essentially no crosslinking agent is present in the tablets of the '545 Patent.

In order to clarify the constituents of a tablet core, Applicants refer to page 3, lines 4-10 of the specification. A tablet core is prepared by the following three steps:

1.) hydrating or drying an aliphatic amine polymer to obtain the desired moisture content;

2.) blending the polymer, the weight of which includes the water of hydration, with excipients such that the polymer comprises at least 95% by weight of the blend; and

3.) compressing the blend to form the tablet core.

From this teaching, it is clear that excipients comprise 0-5% by weight of the tablet core (with the polymer accounting for the remainder of the weight). Suitable excipients include, for example, hardeners, glidants and lubricants (page 4, lines 23-24 of the instant application) and do not include crosslinking agents.

The teachings of the '440 Patent are not considered to be relevant to the instant claims. There is no teaching in the '440 to suggest that a coating appropriate for aspirin, a small molecule, would also be appropriate for a polymer. Also, the '440 Patent does not teach the formulation of a tablet core comprising aliphatic amine polymers. Thus, the '440 Patent does not overcome the deficiencies of the '545 Patent.

Applicants note that it was unexpected that tableting a composition having at least about 95% poly(allylamine) was successful. The instant specification at page 1, line 19 to page 2, line 8 teaches that formulation of a polymer into a tablet is generally not possible without the addition of significant quantities of other materials that assist in the tableting process. Thus, there was no

reasonable expectation that a tablet core containing at least 95% by weight of poly(allylamine) could be made.

In summary, the '545 Patent does not teach a tablet core comprising at least 95% of an aliphatic amine polymer. As discussed above, the weight of a polymer includes the weight of a polymer backbone and any sidechains, along with crosslinking groups and waters of hydration. A tablet core does not contain crosslinking agents. The '545 Patent does not teach a tablet core encompassed within the claimed composition. Therefore, Claims 2-18 are not obvious over the '545 Patent and the '440 Patent. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claim 22 Under 35 U.S.C. 103(a)

A. Summary of the Rejection

The Examiner has rejected Claim 22 as being obvious over the '545 Patent in view of the instant specification at page 10, lines 7-21. The Examiner acknowledges that the '545 Patent does not teach a tablet comprised of a phosphate-binding polymer crosslinked with epichlorohydrin having a hardness from 150-170 N and friability of no more than 0.8%. However, the Examiner states that it would have been in the ability of one of ordinary skill in the art to optimize a tablet to obtain such hardness and friability.

B. Claim 22 Is Not Obvious

Claim 22 recites that at least about 95% by weight of the tablet core is a linear or cross-linked poly(allylamine) or a pharmaceutically acceptable salt thereof. As discussed above, the '545 Patent does not teach tablets having a core comprised of greater than about 95% by weight of a poly(allylamine). Since the '545 Patent does not teach or suggest a tablet having a core with at least about 95% of a poly(allylamine), the preparation of such a tablet core having a hardness greater than about 150 N and a friability of no more than 0.8% with the required poly(allylamine) content is not obvious to one skilled in the art. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If

the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By _____
Jesse A. Fecker
Registration No. P52,883
Telephone: (978) 341-0036
Facsimile: (978) 341-0136

Concord, MA 01742-9133
Dated: January 17, 2003